

Office of HIV and AIDS Malignancy (OHAM) Re-issuance Request



AIDS and Cancer
Specimen Resource

Establishment of the ACSR and Objectives

- The ACSR was established by the NCI in 1994 in response to a BSA Subcommittee assessment of researcher needs in the HIV-associated malignancy field.
- Primary Objective: Meet the specimen needs of clinician and basic researchers in HIV-associated malignancies by ***acquiring, storing and equitably distributing tumor tissues and biological fluids from patients with HIV-associated malignancies.***

ACSR Funds

- A portion of NCI's appropriated funds are restricted for use in HIV-related research. The ACSR is funded using these "AIDS-directed" dollars.
- The NIH Office of AIDS Research (OAR) coordinates the NIH AIDS research program and provides additional oversight and guidance for the use of AIDS restricted funds.
- OAR considers the ACSR a "high priority" project for funding.

Comments on Acquisitions, Curation and Distribution

- HIV-related malignancies encompass a number of rare diseases
- Specimens reflect a wide variety of cancer types
 - Over 20 different diagnosis codes
- Multiple tissue specimen processing types:
 - FFPE, frozen, bloods (PBMC, Plasma, Serum), other bodily fluids (saliva, CVL, urine, CSF), PAP smears
- Multiple time points collected per patient
- Multiple aliquots
- Specimens must be considered in the context of a variety of immunologic and infectious disease states (HIV, KSHV, EBV, HPV). Fortuitous cohort collections with blood specimens that pre-date cancer diagnosis are extremely valuable.
- Tools developed (TMAs, WGA-DNA) to preserve specimen base

ACSR Activity

- Since 2006, 76 different investigators from 50 institutions have received specimens from the ACSR
- 125 publications representing 43 institutions (excluding NCI and ACSR institutions); 11 foreign institutions

	Inquiries	LOIs	Approvals	Disbursement
2008-2011	242	133	119	12,459
2004-2007	123	82	68	4,183

- ACSR has created 24 Tissue Microarrays
 - Disbursed 14,751 TMA cores
- African Collections
 - Acquired: 108,672 samples from 2,245 individuals
 - Disbursed: 5,827 samples

Selected High Impact Research Supported by ACSR

- **Kaposi sarcoma**

- Confirmation of KSHV as the causative agent of KS;
Biology of KSHV and its role in tumorigenesis

Ex: AIDS (1997); Journal of Virology (1997)

- Development of the BCBL-1 primary effusion lymphoma (PEL) cell line. Invaluable research tool with >160 citations in Pubmed.

Nature Medicine (1996)

- Multi-detection algorithm for seroprevalence of KSHV

Journal of Clinical Microbiology (2006)

- KSHV in HIV-suppressed and non-suppressed individuals

mBio (Am. Soc. for Micro. on line journal- 2011)

Selected High Impact Research Supported by ACSR

- **Lymphoma**
 - Novel treatment for Burkitt lymphoma
Blood (2005)
 - Impact of HAART on HIV-associated lymphoma incidence and subtypes in South Africa
Transfusion and Apheresis Science (2011)
- **HIV**
 - HIV-1 spread in tissues of HIV+ individuals
Ex: Blood (2005); *PLoS One* (2011); *Infection, Genetics, and Evolution* (2011)
- **San Francisco Young Men's Health Study**
 - “Rescuing” specimens from this study led to advances in KS and KSHV research
Ex: New England Journal of Medicine (1998); *AIDS* (2004)

Additional Roles of the ACSR and Support of Current and Future Projects

- Serving as AMC Biorepository
- Plays a major role in the HIV+ Tumor Molecular Characterization Project (HTMCP)
- Incoming grant applications for HIV-lymphomas, KS and HPV-related tumors rely on ACSR
- ACSR has written 10 letters of support for investigators submitting grant applications
- A number of funded NCI grants are dependent on the ACSR to achieve research objectives
- At least two, independent, NCI funded clinical trials are relying on the ACSR for curation services for trial specimens

Future High Impact Studies

- A proposed, large clinical trial (over 10,000 screened patients) is planning to use the ACSR as the biorepository for clinical material
- Activities in Sub-Saharan Africa
 - Capacity building
 - Regional Biospecimen Repository
- NCI's Provocative Question #12: Cancers caused by novel infectious agents and mechanisms of tumor induction.
 - ACSR specimens may be a very useful source of material to look for novel infectious agents involved in tumorigenesis

Global HIV-Associated Cancer Burden



- 34 million HIV+ or AIDS pts.
- 70% in resource-limited Sub-Saharan Africa
- High prevalence of oncoviruses that cause HIV-associated malignancies: KSHV, EBV, HPV
- HIV-associated cancers now among the most common tumors in Sub-Saharan Africa
- Lack of adequate pathology; much unknown about types of tumors and epidemiology
- President's Emergency Plan for AIDS Relief (PEPFAR) rollout
- In future, will become more like the US, with less AIDS-defining but more non-AIDS-defining cancers

ACSR and NCI's Global Efforts

- OHAM efforts in Sub-Saharan Africa
 - ACSR
 - AIDS Malignancy Clinical Trials Consortium (AMC)
 - D43 Grants: Developing Research Capacity in Africa for Studies on HIV-Associated Malignancies
- The three initiatives were designed to compliment each other
- ACSR PIs assisting with training and capacity building in pathology and in specimen and data curation, and developing expertise in the challenges regarding obtaining and transporting specimens
- Proposed ACSR repository in Africa

Rationale for Continuing to Acquire New Specimens

- HIV epidemic, and the associated malignancies are ever changing within the USA and globally.
 - Increasing incidence of non-AIDS defining tumors, yet each still a rare disease. Inadequate specimens in repository to meet research needs.
- Fresh frozen specimens needed with matching non-tumor germline samples for comprehensive molecular and genomic analysis
- New specimens needed from the developing world, especially Sub-Saharan Africa. Historical specimens non-existent or of little value.
- New samples needed from patients who have been on long term HAART

Proposed Changes to Enhance ACSR

- Restructuring to enhance cooperation and coordination. Single U01, single PI, broadened membership of the Executive Committee.
- Greater central oversight of collection initiatives, participating sites, collaborations, international activities.
- Flexibility to ensure a more rapid response to exceptional opportunities or poor investments.
- Broader expertise to make more effective scientific decisions.
- Facilitate NCI/OHAM Staff's ability to monitor, and provide guidance and oversight to the ACSR.

Questions?